Pergamon

Tetrahedron Letters, Vol. 38, No. 16, pp. 2887-2890, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00497-8

A Novel One-Pot Conversion of Tetraacetal Tetraoxa-Cages to Aza-Cages Mediated by Iodotrimethylsilane in Acetonitrile

Hsien-Jen Wu* and Jyh-Haur Chern

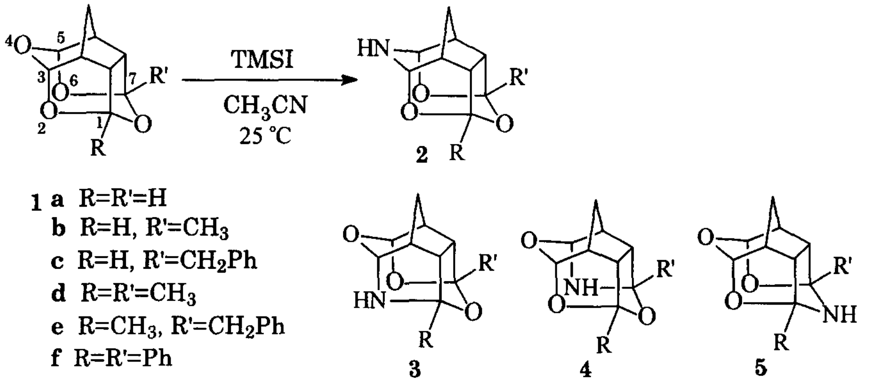
Department of Applied Chemistry, National Chiao Tung University, Hsinchu, Taiwan, China

Abstract: Treatment of the tetraacetal tetraoxa-cages **1a-f** with excess of iodotrimethylsilane in acetonitrile at 25 °C gave the novel tetraacetal trioxamonoaza-cages **2a-f** in 75-80% yields respectively, a novel one-pot conversion of oxa-cages to aza-cages. © 1997 Elsevier Science Ltd.

The reaction chemistry of acetals has been greatly expanded by the use of Lewis acidic promoters particularly in conjunction with silicon-containing nucleophlies.[1,2] Usually, acyclic and monocyclic acetals, especially the acetal groups in monosaccharide derivatives, are the objects for study.[3] Recently, we accomplished the synthesis of novel oxa-cage compounds, such as tetraacetal tetraoxa-cages,[4] tetraacetal pentaoxa-cages,[5] triacetal trioxa-cages,[6] diacetal trioxa-cages,[7] and pentaacetal pentaoxa-cages (the pentaoxa[5]-peristylanes).[8] All these oxa-cages have acetal and ketal groups on the molecule. As part of a program that involves the synthesis, chemistry, and applications of new heterocyclic cages, we report here a novel one-step conversion of oxa-cages to aza-cages mediated by Me_3SiI, leading to formation of novel tetraacetal trioxamonoaza-cages. To our knowledge, a one-pot conversion of acetal group to monoazaacetal group mediated by Me_3SiI has not yet been reported.[1,2]

Reaction of the tetraacetal tetraoxa-cages **1a-1f** with three equivalents or more of iodotrimethylsilane in acetonitrile at 25 °C for 4 h gave the novel aza-cages **2a-2f** in 80-85% yields (Scheme 1). This novel conversion takes place regioselectively on the C(3)-O(4) or O(4)-C(5) bond. No detectable amount of the other regioisomers **3**, **4**, or **5** was obtained. We attribute the highly regioselective oxygen-nitrogen conversion reaction to the unusually large bond angle of C(3)-O(4)-C(5) of the tetraoxa-cages 1. While the other C-O-C bond angles of these tetraoxa-cages are in between 111°-108°, the C(3)-O(4)-C(5) bond angle is 117.5°, remarkably larger than the ordinary bond angles with sp^3-hybridized atoms.[4a] The stability and size of the ring may also be an important factor for the high regioselectivity. In the case of **1a**, only **2a** was obtained. Thus, the steric factor for the regioselective conversion was excluded. Reaction of **1** with excess of chlorotrimethylsilane in acetonitrile at 25 °C remained unchanged. The structure of the aza-cages **2a-2f** was finally proven by X-ray analysis of the crystalline compound **2d** (Figure 1). The conformation of the nitrogen atom with respect to the apical carbon atom was shown to be in a boat form. The bond angle of C(3)-N(4)-C(5) is 119.5°.

Scheme 1



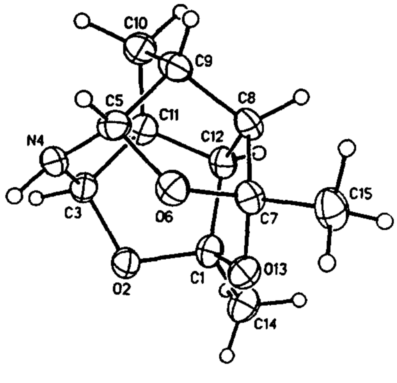
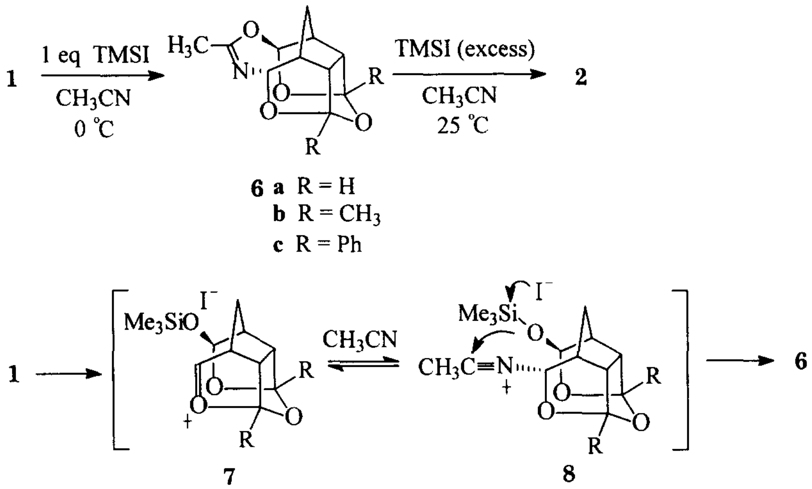


Figure 1. ORTEP diagram of **2d**

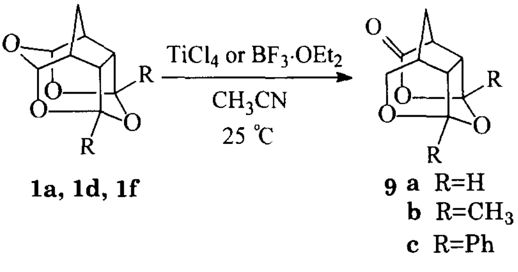
Reaction of **1a**, **1d**, and **1f** with one equivalent of Me_3SiI in acetonitrile at 0 °C for 2 h gave the ring expansion products **6a-6c** in 85-90% yields (Scheme 2). Treatment of **6a-6c** with excess of Me_3SiI in acetonitrile at 25 °C gave the aza-cages **2a**, **2d**, and **2f** in 80% yields. Thus, the ring expansion compound **6** is the intermediate of the conversion of oxa-cage **1** to aza-cage **2**. The proposed mechanism for this interesting reaction involves a Ritter-type reaction[9] of the oxonium ion **7** with acetonitrile via the nitrilium ion **8** to give the intermediate **6**.

Scheme 2



Reaction of **1a**, **1d**, and **1f** with Lewis acids, such as $TiCl_4$ and $BF_3{\cdot}OEt_2$, in acetonitrile at 25 °C for 4 h gave the hydride rearrangement products **9a-9c** in 80% yields (Scheme 2). No detectable amount of the corresponding aza-cages **2a**, **2d**, and **2f** was obtained. We attribute the highly regioselective hydride rearrangement to the unusually large bond angle of C(3)-O(4)-C(5) of the tetraoxa-cages 1. In the case of **1a**, only **9a** was obtained.

Scheme 3



Acknowledgment: We thank the National Science Council of the Republic of China for financial support (Grant No. NSC85-2113-M009-004). We also thank Dr. S. L. Wang and Miss F. L. Liao (at the Department of Chemistry, National Tsing Hua University) for their help in carrying out X-ray crystallographic analysis.

References

1. For reviews: (a) Mukaiyama, T.; Murakami, M. *Synthesis* **1987**, 1043. (b) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941.
2. (a) Mukaiyama, T.; Hayashi, M. *Chem. Lett.* **1974**, 15. (b) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295. (c) Kende, A. S.; Johnson, S.; Sanfilippo, P.; Hodges, J. C.; Jungheim, L. N. *J. Am. Chem. Soc.* **1986**, *108*, 3513. (d) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107. (e) Mori, A.; Ishihara, K.; Yamamoto, H. *Tetrahedron Lett.* **1986**, *27*, 987. (f) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113*, 8089. (g) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1991**, *56*, 6458.
3. (a) Ratcliffe, A. J.; Konradsson, P.; Fraser-Reid, B. *J. Am.Chem. Soc.* **1990**, *112*, 5665. (b) Pavia, A. A.; Ung-Chhun, S. N.; Durand, J. L. *J. Org. Chem.* **1981**, *46*, 3158. (c) Gordon, D. M.; Danishefsky, S. *J. Org. Chem.* **1991**, *56*, 3713. (d) Sano, H.; Mio, S.; Tsukaguchi, N.; Sugai, S. *Tetrahedron* **1995**, *51*, 1387. (e) Noort, D.; van der Marel, G. A.; Mulder, G. J.; van Boom, J. H. *Synlett* **1992**, 224.
4. (a) Wu, H. J.; Lin, C. C. *J. Org. Chem.* **1995**, *60*, 7558. (b0 Wu, H. J.; Lin, C. C. *J. Org. Chem.* **1996**, *61*, 3820. (c) Wu, H. J.; Huang, F. J.; Lin, C. C. *J. Chem. Soc., Chem. Commun.* **1991**, 770. (d) Lin, C. C.; Wu, H. J. *J. Chin. Chem. Soc.* **1995**, *42*, 815. (e) Lin, C. C.; Huang, F. J.; Lin, J. C.; Wu, H. J. *J. Chin. Chem. Soc.* **1996**, *43*, 177. (f) Lin, R. L.; Wu, C. Y.; Chern, J. H.; Wu, H. J. *J. Chin. Chem. Soc.* **1996**, *43*, 289. (g) Wu, H. J.; Chern, J. H.; Wu, C. Y. Submitted for publication.
5. Lin, C. C.; Wu, H. J. *Synthesis* **1996**, 715.
6. Wu, C. Y.; Lin, C. C.; Lai, M. C.; Wu, H. J. *J. Chin. Chem. Soc.* **1996**, *43*, 187.
7. (a) Wu, H. J.; Tsai, S. H.; Chung, W. S. *J. Chem. Soc., Chem. Commun.* **1996**, 375. (b) Wu, H. J.; Tsai, S. H.; Chung, W. S. *Tetrahedron Lett.* (in press)
8. Wu, H. J.; Wu, C. Y. submitted for publication.
9. (a) Senanayake, C. H.; Roberts, F. E.; DiMichele, L. M.; Ryan, K. M.; Liu, J.; Fredenburgh, L. E.; Foster, B. S.; Douglas, A. W.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J.; *Tetrahedron Lett.* **1995**, *36*, 3993. (b) Ritter, J. J.; Minieri, P. P. *J. Am. Chem. Soc.* **1948**, *70*, 4045. (c) Bishop, R. *Comprehensive Org. Syn.* **1991**, *6*, 261.

(*Received in China* 9 *October* 1996; *revised* 5 *December* 1996; *accepted* 24 *January* 1997)